specific gravity of only 1006 or 1008, and contained a small proportion of albumen. On another occasion a similar attack was accompanied by slight left hemiplegia, with marked impairment of articulation; and, in my absence, two distinguished colleagues, not aware of the previous history, came to a diagnosis of advanced Bright's disease, and gave a most unfavourable prognosis. On both occasions a dose of calomel put an end to the serious symptoms almost at once—the hemiplegia, of course, excepted, which only disappeared very gradually.”

8. Gangrene of the extremities and (9) angina pectoris are symptoms which have occurred in other cases of arterial hypermyotrophy, but they were not present in the above.

The existence of enlargement of the heart in cases of arterial hypermyotrophy renders it necessary to diagnose this condition from the other causes of cardiac hypertrophy; but the presence of vertigo, thickened arteries, and the other symptoms above mentioned, together with the absence of the signs belonging to any of the other causes of cardiac enlargement, enable one to come to a conclusion. There is every reason to believe that cases of arterial hypermyotrophy are very frequently mistaken for cases of cardiac-valvular disease. When, in the former condition, ventricular dilatation has supervened, it gives rise to a systolic apical murmur which throws the physician off his guard, and in any case renders the diagnosis a task of extreme difficulty. In none of the cases of arterial hypermyotrophy which I have met with has dropsy ever been present, and this fact may be of some assistance. The pulse usually is slow and regular, but when cardiac failure supervenes, one of its earliest manifestations is a rapid and irregular pulse. It is not possible to make more than the briefest reference to these matters on the present occasion.

TREATMENT.

Space does not permit me on the present occasion to go fully into the question of treatment; but it will be gathered from these two cases that one of the chief indications in arterial hypermyotrophy is the reduction of high arterial tension. To this end saline purgatives and a dose of calomel are often of use, and even the extreme measure of bleeding may be called for, and may result, as in the first case, in very prompt relief. The value of rest is also illustrated in both of these cases, either alone or, as in the second, combined with massage and passive movements, to relieve the overburdened heart. In the earlier stages of the affection Schott baths and exercises may be resorted to, though caution is required in cases where there are reasons for suspecting advanced atheroma. For the giddiness and dyspnoea nitroglycerine seems to be the sovereign remedy, and it not only promptly relieved but also prevented this symptom very markedly in both of the above cases.

The matters here so cursorily dealt with will receive more exhaustive consideration on a future occasion. These two cases are only published in the hope that, by the recognition of what I am persuaded is a frequent and independent disorder, cases may accumulate and thus light may be thrown on what is admittedly one of the most difficult sections of pathology.

REMARKS ON

A CASE OF

RECURRENT SARCOMA OF THE MAMMARY GLAND

TREATED BY

COLEY'S FLUID

WITH A FATAL RESULT.

By A. MARMADUKE SHEILD, M.B., F.R.C.S.,

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PREVIOUS HISTORY OF THE CASE.

A NURSE, aged 44, was admitted into St. George's Hospital on April 3rd, 1896, and was kindly placed under my care by Mr. Pick, who had previously operated upon her. In January, 1896, the left breast was removed for a rapidly-growing malignant tumour, which on microscopical examination proved to be a myeloid sarcoma of a very pronounced type. The axilla was at that time apparently free. Within six

weeks of the operation, the wound having healed, the disease returned in the scar, in the axilla, and beneath the clavicle. The patient attended in the out-patient department, and week by week the disease perceptibly increased, so that she was only too anxious to try any form of treatment that might afford a chance of relief. She suffered some pain of a "shooting" nature in the breast and down the arm.

On her admission, it was noted that there were two masses of disease in the centre of the scar. One was the size of a large walnut, livid, and marked by enlarged veins; the other was somewhat smaller, and was on the point of fungating. A large mass of disease was situated under the pectoral muscle. The general health and nutrition were good, and there was no evidence of deposits of disease elsewhere.

EFFECTS OF THE INJECTIONS.

The injection treatment was commenced on April 3rd, when 1 minim of Coley's fluid, which, I may add, is a mixture of the toxins of the streptococcus of erysipelas and the bacillus prodigiosus, was thrown into the larger nodule at 4.40 P.M. At 6 P.M. the patient had a slight rigor and felt ill with a headache; a faint roseate blush spread over the skin round the site of injection. At 10 P.M. the patient was comfortable again, and the "blush" on the skin had extended as far as the clavicle. The pulse was quickened, and the temperature had risen 1° F.

On April 4th the same treatment was carried out at the same hour. Two minims of the fluid were injected into the same growth. The reaction symptoms were more severe, the rigors were pronounced, and the temperature was raised to 102.6° F. The pulse was quickened and feeble, and a red blush extended round the site of injection as before. She also complained of some numbness of the hands and feet.

On April 5th the temperature had again become normal, and the patient was asleep and comfortable. She volunteered the statement that the pain in the growth was greatly relieved. Two minims of the fluid were again injected. There was no reaction after this injection.

On April 6th the patient complained, however, of numbness of the hands and feet, and herpes appeared on the lips in the morning. At the usual hour 3 minims of Coley's fluid were injected. The patient within an hour had severe shivering, and the temperature rose to 103° F. She felt giddy and faint, with the usual "numb" feelings in the extremities.

On April 7th no injection was given. The patient was fairly comfortable, but felt very weak. The larger tuber of growth had completely altered its colour, being of a roseate hue, and obviously inflamed.

On April 8th an injection of 3 minims was again carried out, but slight reaction followed. The tumour was obviously smaller and flatter.

On April 9th and 10th the injection was followed by no reaction, so on April 11th and 12th 6 minims were injected beneath the clavicle into the masses of growth in this situation. Beyond slight local redness and pain no constitutional symptoms followed. I determined to omit the injections for a week, to allow the patient's general condition to improve, and to note the effect that had been produced.

On April 13th it was noted that the larger growth in the scar had discharged freely through a small opening; it was considerably smaller. The patient expressed herself as much relieved of the pains she had previously suffered from.

On April 20th the larger growth had entirely disappeared, its site being represented by a horny discoloured patch of thickened integument. The smaller tumour was semi-necrotic. The mass beneath the clavicle appeared less prominent. Six minims of the fluid were injected into the smaller tumour. The injection was made at 5.30 P.M. At 6.30 a rigor was experienced, and the pulse was quickened; the temperature was raised to 100.2° F.

On April 21st 6 minims were injected into the same growth. Well-marked reaction with a rigor occurred, and the temperature rose to 103.8° F.

On April 22nd a second rigor occurred, and the temperature after it rose to 103°. The patient was very ill and prostrate, and the temperature did not come down. On April 23rd and 24th the symptoms were very serious. At 10 A.M. on April 23rd the temperature was 105°, the pulse 140, and the respirations 50 in number. Small pustules appeared on the legs,

with petechial spots on the abdomen, and the patient became very comatose and drowsy. On April 24th she became quite unconscious, and died about 3.15 P.M. There appeared to be a good deal of local inflammation in the site of the growth, and shortly before death petechiæ appeared upon the face.

THE CHARACTERS OF THE FLUID USED FOR INJECTION.

It may be here especially noted: (1) That the fluid was cultivated by Dr. Slater, and proved sterile. (2) That just after the last injection an injection of equal magnitude was made in a case of carcinoma, with but slight effects; the fluid was taken from the same bottle. (3) The fluid was obtained from the British Institute of Preventive Medicine, and was prepared by mixing the toxins of erysipelas and the bacillus prodigiosus. It was twice cultivated and found to be sterile.

The general treatment of the case may thus be summarised. Stimulants were freely given, and the patient's general health well supported. When the serious symptoms appeared towards the close of the case, cold sponging was resorted to to attempt to reduce the hyperpyrexia, and at the last, when respiratory embarrassment became evident, liquor strychninæ was administered. The injections were carried out with the same syringe, always carefully sterilised by boiling before use.

SUMMARY OF RESULTS.

A summary of the symptoms observed in this case would be as follows: Smart reaction followed the first two injections. After that three injections made in increasing quantities failed to have effect. After a week's interval severe reaction was again established. The effect on the growth injected was certainly very marked. It caused its undoubted shrinkage and apparent disappearance. This seemed due purely to inflammatory action in a soft neoplasm, rather than to any purely specific action of the fluid itself. The fatal end of the case will be discussed after the *post-mortem* appearances are described.

POST-MORTEM APPEARANCES.

At the *post-mortem* examination, conducted by Dr. Rolleston, signs of general pyæmia were apparent. Thus secondary abscesses and infarcts were found in the liver, myocardium, kidneys, and right knee-joint. The growth beneath the clavicle was necrotic, and it was particularly important to note that beneath the site of the two nodules which had disappeared was some purulent infiltration of the thoracic muscles. A bacteriological examination was kindly performed by Dr. Russell Wells, and the staphylococcus aureus was found in the secondary abscesses. This is noteworthy, as the original fluid was prepared from streptococci. There were no visceral deposits of sarcoma.

REMARKS.

I have thought it right to record this case because it well illustrates the difficulties and dangers that attend methods of treatment the effects of which may easily spread beyond our control. Fortunately in this case the serious nature of the disease justified the employment of a perilous mode of treatment. The patient could not long have survived, but it is right to allow that her life was undoubtedly shortened by the treatment. Nevertheless, so marked was the effect produced upon the prominent masses of growth that I would not hesitate to advise this treatment in cases of sarcoma which appear hopeless for less risky modes of treatment. It is especially interesting to note that the same fluid, in the same doses, was used for another patient suffering from carcinoma with little or no reaction result. The injections were made with scrupulous care, with an aseptic syringe, under my immediate direction. The fluid was found to be sterile. Hence the fatal organisms probably developed in the necrosing tissues of the growths themselves, and the "flaw" in this case was possibly due to imperfect disinfection of the skin. Little has hitherto been done with the seropathy of malignant growths in this country. From America we have the most conflicting testimony. For instance, Professor Senn¹ reports nine cases of failure, and says that the method is of no value, whereas the successful results claimed by Coley are well known,² and some of his cases are truly remarkable. An

excellent paper by Repin³ well sets forth the present status of the serum treatment of these cases. There can be no doubt that remarkable results in the disappearance of sarcomata have been brought about by some of these surgeons. Butlin, in a clinical lecture delivered at St. Bartholomew's Hospital on December 11th, 1895, seemed to think that the method was useless in carcinoma, but might prove of some benefit in sarcoma. The method is worthy of more extensive trial in this country, and the case I have related shows the importance of making every attempt, at all events, to prevent the entrance of dangerous organisms into the inflamed neoplasms.

Dr. Slater, our bacteriologist at St. George's Hospital, to whom I am indebted for much information on this subject, thus classifies the agents at present employed:

(a) Injection with the virulent organism apparently effective, but certainly dangerous.

(b) Treatment with toxins, occasionally successful, but giving rise to very severe symptoms.

(c) Treatment with the toxic blood serum of an infected animal, of doubtful efficacy, but giving rise to less constitutional disturbance.

(d) Antitoxic serum, free from risk, but apparently ineffective.

Thus it would appear that the more virulent the fluid the more marked is the effect upon neoplasm, and curative action in the growth and danger to life are in direct proportion. This is only what one would from analogy expect. It is after smart and dangerous attacks of erysipelas that retrogression of malignant growths has been observed most strikingly, and which led to the experiments of Ricord and Fehleisen, who in 1882 attempted to inoculate with living cultures of erysipelas.

I have received the following note on the preparation of Coley's fluid from Professor Macfadyen:

"Flasks containing nutrient broth are inoculated with a virulent culture of the streptococcus erysipelatis, and incubated at 30° to 35° C. for three weeks. The same flasks are then inoculated with the bacillus prodigiosus, and kept at room temperature for ten to twelve days. The mixed culture obtained is heated up to 50° or 60° C., with a view of killing the micro-organisms. A small quantity of carbolic acid is added to the sterilised broth, and it is used without filtration, commencing with small hypodermic doses of not more than half a minim."

REFERENCES.

- ¹ *Journal Amer. Med. Assoc.*, July 27th, 1895. ² *Amer. Journ. Med. Sci.*, July, 1894. ³ *Revue de Chirurgie*, June, 1895.

ON THE ACTIVE CONSTITUENT OF THE THYROID GLAND.

By ROBERT HUTCHISON, M.D.,

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A few months ago I published in the *JOURNAL*,¹ a preliminary note, in which I stated that the colloid matter of the thyroid is the only active part of the gland therapeutically. Since then I have published in the *Journal of Physiology*,² a paper dealing fully with the chemistry of the thyroid in which the above conclusion is supported by evidence drawn from the results of experiments upon dogs. In the present article I wish to present the clinical evidence by which I believe my conclusions to be finally proved.

For the sake of clearness it will be well to begin with a brief summary of the chief facts in the chemistry of the thyroid. I have shown that the proteids of the gland are two in number:

1. A *nucleo-albumin* present in small amount, and probably derived from the cells lining the acini.

2. The *colloid matter*, which possesses certain striking chemical peculiarities. One of these is that it contains, in addition to phosphorus, a considerable quantity of iodine. Another is that on gastric digestion it readily splits into two parts—a proteid part which yields albumoses and peptone, and a small insoluble residue which is entirely proteid free.

¹ *BRITISH MEDICAL JOURNAL*, March 21st, 1896.

² *Journal of Physiology*, vol. xx, p. 474.